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BENZOIC *VS.* CINNAMIC ACID IN FOOD ANALYSIS.

By Wilbur L. Scoville.

An indictment was recently served in Massachusetts against a prominent firm for selling sweet pickles which were said to be preserved with benzoic acid. Both the Government chemist and the chemist to whom the sealed samples were taken, said that benzoic acid was present. The manufacturer denied this strenuously, and asked for an investigation by the writer, which investigation brought out the following facts:

The pickles were highly flavored, oils of cinnamon and clove being the chief flavoring agents. Oil of cinnamon (cassia) is composed chiefly of cinnamic aldehyde, which oxidizes on exposure to cinnamic acid. Old oils of cinnamon may be found containing abundant crystals of this acid.

Cinnamic acid resembles benzoic acid closely, both in physical and chemical properties. So close is the resemblance that in the early part of the nineteenth century the two acids were confounded, and until Bizio, in 1826, showed that cinnamic acid is a distinct substance, it was identified with benzoic acid.

The resemblance between the two acids appears to have been overlooked in the above case.

For the detection and identification of benzoic acid two tests have been adopted by Government chemists. These are (1) the ferric chloride test, which gives a flesh-colored precipitate with neutral benzoates, and (2) the metadinitrobenzoic acid test, which consists in heating the dry substance (after separation from other material) with strong sulphuric acid and a little potassium nitrate, neutralizing

the fluid with ammonia water, and adding a drop or two of ammonium sulphide solution, when a red color appears if benzoic acid was present.

Neither of these tests will distinguish between benzoic and cinnamic acids. In fact, cinnamic acid responds to both tests almost as well as benzoic.

With ferric chloride, in moderately strong and colorless solutions, cinnamic acid gives a precipitate that is decidedly yellowish, and is distinguishable from benzoic. But in weak solutions, when the precipitate is slight, yet marked, the precipitates cannot be distinguished by color, and when the test is applied to a deeply colored solution, as is obtained from sweet pickles, it is obvious that a test depending upon a tint cannot be trusted.

Some oil of cinnamon (both cassia and Ceylon cinnaman oils were used in separate tests) was shaken with warm water and the liquid filtered. A drop of ferric chloride added to a test-tube full of the filtrate produced a precipitate that could not be told, by color or physical appearance, from that produced in a weak solution of sodium benzoate by ferric chloride. Yet the conditions of the test were most favorable for comparing results. Some cinnamon water was distilled with steam, the distillate neutralized with ammonia, evaporated to a small volume, rendered acid, shaken out with ether, the ethereal solution shaken with water, then with weak ammonia solution, and the excess of ammonia driven off by evaporation on a water bath. This solution gave a precipitate with ferric chloride that might fairly be taken for benzoic acid; and this process was the one used by the Government chemist, and upon which the indictment was based.

Some cinnamic acid was prepared by oxidizing oil of cassia with hydrogen peroxide, and the purified acid (having a melting point of 133° C.), reacted to both the iron and the ammonium sulphide tests in a way similar to benzoic acid.

It is obvious that these tests cannot be relied upon to detect benzoic acid in a product that is flavored with cinnamon.

The best test found for distinguishing between the two acids is the manganous test. Manganous salts give a white precipitate with cinnamates, which gradually becomes crystalline. No precipitate is found with benzoates, even in moderately strong solutions.

The precipitate forms slowly with cinnamates, but is quite delicate

The solution should be allowed to stand an hour, at least, with moderately weak solutions.

Oil of cinnamon is a frequent condiment in food products, and the above shows clearly that when these are examined for benzoic acid, the cinnamon is likely to mislead. If a crystalline body is obtained in the process of separating, the usual tests cannot be relied upon to distinguish between the two acids. It is difficult to get the acid in a pure enough condition to identify it by the melting-point, and the sublimation test is also unreliable.

If a precipitate is obtained with ferric chloride in neutral solution, the liquid should also be tested with solutions of manganous sulphate (or chloride). A precipitate with this, after an hour's standing, shows cinnamic acid. If no precipitate occurs benzoic acid is indicated.

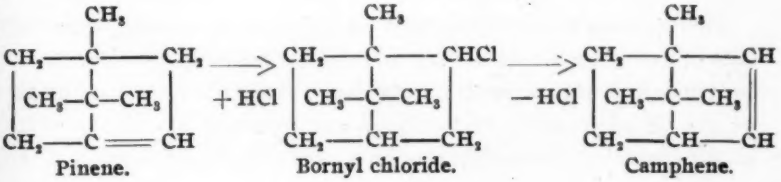
SYNTHETIC CAMPHOR.

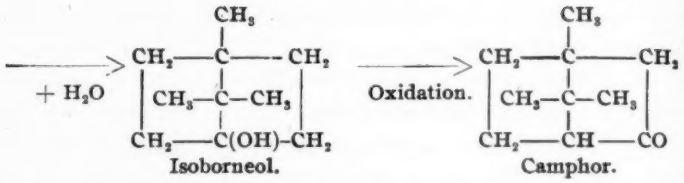
By Frank Tutin.

In the August number of this Journal, pp. 349–356, there appeared a contribution from Mr. L. F. Kebler (Chief of the Drug Laboratory, Washington, D. C.), entitled "Synthetic Camphor," which was intended by the author to be a response to the requests received by the Bureau of Chemistry for information on this subject.

In the above-mentioned communication an account was given of the various processes which have been devised for the synthetic production of camphor, and the chemical changes involved therein were illustrated by means of structural formulæ. In view of the purpose which the paper was intended to serve, it appears somewhat unfortunate that it should contain a number of inaccuracies, and as these are so fundamental in their nature, it would seem desirable that attention should be drawn to them.

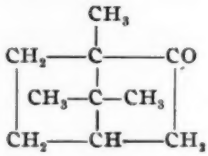
The author, for example, has represented the changes involved in the conversion of pinene into camphor by means of the following formulæ:



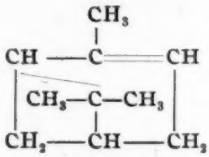


Isoborneol. Camphor.

The first criticism that may be made regarding the above formulæ is that the one assigned to camphor is incorrect. It has been shown, namely, by Bredt (*Ber. d. deutsch. chem. Ges.*, 1893, **26**, 3047) and subsequent workers, that this ketone is represented as follows:



In the second place, the formula given for isoborneol is obviously impossible, for this substance is represented as a tertiary alcohol, and could not, therefore, afford camphor on oxidation. The correct structural formula for isoborneol, and also for borneol, since the latter only differs from the former stereochemically, is obtained by substituting for the oxygen atom in Bredt's camphor formula the elements HOH. Camphene and bornyl chloride are correctly represented, but the structure assigned to pinene is not that which is at present accepted. The formula by which Mr. Kebler represents this terpene is that which was suggested by Bredt in 1893 (*loc. cit.*), but the more recent work of Wagner (*Ber. d. deutsch. chem. Ges.*, 1894, **27**, 1636) and of Baeyer (*Ibid.*, 1896, **29**, 3, 326, 1907, 1923, and 2775) indicates that pinene possesses the following structure:



This formula is now generally accepted as the correct representation of the constitution of pinene. It consequently follows that the conversion of this terpene into bornyl chloride is not brought about by the simple addition of hydrogen chloride, but involves the change of the dimethyltetramethylene into a trimethylpentamethylene ring.

A further striking inaccuracy occurs on page 353 of Kebler's paper. He there represents the formation of camphor from "turpentine" by means of oxalic acid, but in this case pinene and camphor are represented by formulæ which are not only totally different from those assigned to these substances in the preceding portion of his paper, but are, moreover, quite incorrect.

It may incidentally be noted that the same error regarding the structure of pinene as that first referred to above occurred in a paper entitled "Syntheses of Camphor," recently communicated to the New York section of the Society of Chemical Industry. (*J. S. C. I.*, 1907, Vol. XXVI, **8**, 384.)

THE WELLCOME CHEMICAL RESEARCH LABORATORIES,
LONDON, E. C.

COMMENTS ON SOME OFFICIAL STANDARDS AND TESTS.[1]

BY L. HENRY BERNEGAU.

In commenting upon some official standards and tests it has been thought best to bring before the meeting this evening a few selected observations somewhat out of the usual run, rather than to consider the more familiar tests, such, for instance, as are included in the "purity rubric" requirements, which must now be well known to all of us whose daily duties demand a constant use of the United States Pharmacopœia. I shall, therefore, confine my comments to less than half a dozen topics, hoping that the experiences of others present may be brought out in the discussion, for it is only by working together and exchanging our views that real good may come from these meetings, and the scientific status of the professsion of pharmacy be raised.

Gum Benzoin.—The U.S.P. requires that benzoin be soluble in 5 parts of warm alcohol, show an acid reaction to litmus paper, be soluble in KOH and NaOH solutions, on incineration leave not more than 2 per cent. ash and yield benzoic acid on sublimation.

There are four kinds of benzoin on the market—Siam, Sumatra, Penang and Palemga varieties. The first two are the ones with

[1] Read before the Philadelphia Branch of the American Pharmaceutical Association, November, 1907.

which we mostly have to deal. Siam benzoin should be nearly free from cinnamic acid; Sumatra sometimes contains a considerable amount of it. Siam benzoin contains about 0·15 per cent. vanillin; Sumatra benzoin contains on the average about 1 per cent. Although the percentage of vanillin in the Sumatra varieties is therefore six to seven times higher than in the Siam variety, the latter has a more pronounced vanilla-like odor. We received lately a refined gum benzoin of an extraordinarily strong vanilla-like odor, and suspecting a cheap resin flavored with vanillin we took special care in testing the same. The sample was of a dark-reddish brown color, brittle and translucent, almost perfectly soluble in 5 parts of warm alcohol and also soluble in KOH solution. It was nearly free from cinnamic acid—there as cinnamic-phenyl-propyl ether and cinnamic-benzyl-ether (test made with potassium permanganate)—and left only 0·58 per cent. ash on incineration. An assay for benzoic acid, made by sublimation, gave 11·74 per cent., the average of the latter being about 10 per cent. in a good quality benzoin (bisulphite method being used). Although the vanillin odor, as said before, was extremely strong, we evidently had not an adulteration but a high-grade quality before us, probably refined Siam benzoin with a small percentage of Sumatra benzoin.

ESSENTIAL OILS.

In many cases the different oils stood the U.S.P. tests for specific gravity, solubility, general appearance, odor, etc., but did not answer U.S.P. requirements in regard to optical rotation. For example:

Oil of Coriander had a specific gravity of 0·87 at 25° C., solubility, etc., was O. K., but the optical rotation at 25° C. was — 15·4, instead of + 7° to + 14°

Oil of Thyme was O. K. in regard to specific gravity, solubility, etc., and was free from official phenol. The oil assayed 23 per cent. phenols, 3 per cent. more than the U.S.P. requires. The optical rotation, however, was + 9·5, the U.S.P. requiring the oil to be slightly laevogyrate.

In testing *Oil of Orange*, *Oil of Anise*, and others, we found the same conditions.

Oil of Eucalyptus we found to have the required optical rotation, but the percentage of cineol was in most cases too low, some oils assaying only 10–15 per cent. instead of 50 per cent.

Oil of Sandalwood we found U.S.P. with a high percentage of santalol and in all (15) except two samples, the optical rotation was between — 16° to — 20°, according to U.S.P. The two other samples read — 10.5° and — 11·2°, respectively. Both assayed about 91 per cent. santalol.

We are making at present tests of this important drug by fractional distillation and shall be glad to make our results public later.

Under *Oil of Anise* the U.S.P. says: "The oil should be laevogyrate, the angle of rotation being — 2° in a 100-mm. tube at 25° C. (absence of oil of fennel)." Looking up oil of fennel in the U.S.P. you will find not a word on the optical rotation of the oil—not even mentioned whether it should be dextro- or laevogyrate. The question is, "Would the angle of rotation be increased or decreased by the presence of oil of fennel"? What is the reason for omitting the angle of rotation in one case and giving it in another?

Nitroglycerin.—In assaying nitroglycerin in solutions as well as in tablets we use Lunge's Nitrometer with the best results in determining the exact amount of absolute glyceryl trinitrate. It takes a little experience to work the nitrometer quickly, but once acquainted with it, it is easy to make five or more different determinations in one hour. We assayed recently quite a number of samples of spirits of glonoin, sold to contain 10 per cent., and found on the average only 8·5 per cent. absolute nitroglycerin by weight. As these spirits enter all preparations containing nitroglycerin, it is necessary to determine their absolute strength before using them. Tablets made with glonoin lose 30 to 40 per cent. in strength during manufacturing, and it is necessary to allow a large excess to bring the finished tablets to a required strength. The tablets seem to lose during the granulation process, probably by evaporation, as granulations ready for the tablet machines, and the finished tablets themselves, were found to contain the same amount of nitroglycerin. The age does not seem to have much effect on the tablets because a number of lots assayed nine months ago show the same respective amounts of nitroglycerin now.

Potassium Arsenite.—In assaying potassium arsenite powder for arsenous acid care should be taken to use the right formula. The appendix of the U.S.P., under "List of the elements and principal pharmacopœial chemicals," gives the formula for potassium arsenite

as $KAsO_2$. This formula is correct, if we make a solution of the salt by gently heating As_2O_3 with an excess of potassium bicarbonate in the presence of water, as in the case of the official Liq. Pot. Arsenitis, but it is not correct for the dry salt, which has the formula $KAsO_2 + HAsO_2 + H_2O$. (E. Schmidt, Merck's Index, etc.) Taken as $KAsO_2$ the salt would contain about 68·4 per cent. As_2O_3, but taken as $KAsO_2 + HAsO_2 + H_2O$, it contains about 72·7 per cent. As_2O_3.

The dry salt is difficult to manufacture and contains always a more or less large amount of potassium carbonate—one of our samples running as high as 35 per cent. K_2CO_3 and only 38 per cent. of As_2O_3. As_2O_3 was determined by the common Iodine method, the K_2CO_3 by calculation from CO_2 found with Scheibler's apparatus (for determination of CO_2 in boneblack).

ANALYTICAL LABORATORY OF THE H. K. MULFORD COMPANY,
November 5, 1907.

THE OPSONIC THEORY AND BACTERIAL VACCINES.

BY A. PARKER HITCHENS, M.D., Glenolden, Pa.

For the more lucid understanding of a theory which occupies only a small part of an important branch of medical science, some knowledge of the fundamental principles of the general subject is essential. This is the relation which the opsonic theory bears to that most interesting and apparently inexhaustible subject—immunity; and I therefore request your indulgence while I consider it briefly.

Immunity may be roughly defined as resistance to disease. This immunity or resistance may be natural, congenital or acquired; man is *naturally* immune to certain diseases which attack the lower animals (black leg, hog-cholera). A child may be born with a degree of inherited immunity to a certain disease—*congenital;* immunity to a disease is *acquired* by recovery from an attack of the disease or by artificial inoculation. Immunity is relative or absolute. Immunity is *active*, when the body of the individual elaborates its own protective, or curative substances; it is *passive* when the protective or curative substances are manufactured in the body of another animal and transferred artificially (antitoxin).

The study of immunity, the foundation of which was laid by Pasteur and Koch, modest in its beginnings, has grown to be, in my opinion, the most important of all sciences. The application of principles evolved from investigations in immunity has resulted in the lengthening of the average life of man by several years, and we have not yet begun to fathom its possibilities.

Since the time of Pasteur many theories have been evolved to explain the mechanism of our resistance to communicable disease.

Attempts have been made to satisfy our curiosity as to why one has scarlet fever, as a rule, but once; why a single attack of typhoid fever endows one with the power of drinking Schuylkill water with impunity; why a successful vaccination protects against smallpox. One of the early hypotheses is that known as the "Exhaustion Theory." Of this the following illustration has been given: a man coming from market with a number of different kinds of fruit in his basket is attacked by several boys. One boy who is fond of no fruit but apples eats all the apples, another who cares only for peaches eats all the peaches, the third who has a taste for bananas alone exhausts the supply of this fruit, and so on. In other words during an attack of typhoid fever, for example, some substance in the normal body is "eaten up" by the typhoid bacillus, and the individual is henceforth immune to this disease. After much discussion and experimentation this theory of Pasteur's was found to be untenable.

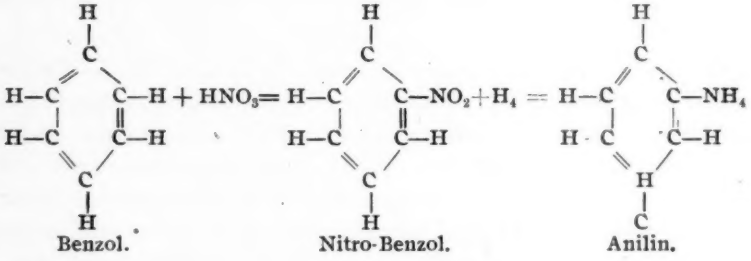
Next the "Retention Theory" attracted much notice. This is just the opposite of the exhaustion theory, in that, instead of taking something away from the body, certain materials were supposed to be added by the growth of infective bacteria in the tissues.

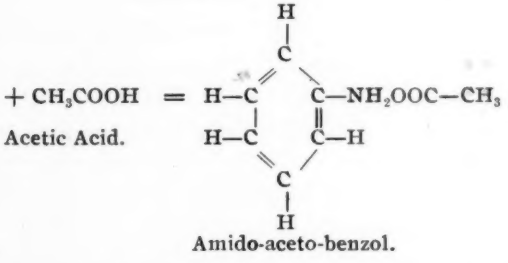
The two theories that have occupied the field for the last few years are the side-chain theory of Ehrlich and the phagocytic theory of Metchnikoff. According to the latter, bacterial diseases are resisted by the leucocytes—the white blood corpuscles. When one of these meets a bacterium, it encloses and ingests it and may kill it. If the germ is very strong or virulent the leucocyte may not be able to kill it, but may itself be killed. When the leucocytes are unable to destroy invading organisms an infection results. The process of the ingestion of bacteria by the leucocytes is called phagocytosis, and the white-blood corpuscles performing this function are called phagocytes.

The side-chain theory of Ehrlich is not so easy of explanation, it

is essentially a chemical one. He believes that the mechanism of immunity is allied to the phenomena of nutrition of the body cells.

For its nutrition each body cell is believed to be endowed with radicals possessing side chains or bonds of affinity; of this the benzol ring is the classic illustration. The formula for benzol is C_6H_6. Written out graphically we find each atom with its bonds of affinity perfectly satisfied. With certain chemicals, however, one of these hydrogen atoms may be split off and other elements linked to the radical. The changes which take place in the building up of acetanilid amply illustrate the variety of substances physically different which may exist without the slightest change in the benzol ring.





Amido-aceto-benzol.

The number of different molecular groups which may link themselves to this side chain reaches almost to infinity.

The analogy between this view and that of Ehrlich concerning cellular nutrition and the production of acquired immunity is very close. The cell is believed to select its nourishment by means of side chains, but instead of being chemical they are protoplasmic side chains. These protoplasmic side chains are called receptors. Now, cells have receptors not only for substances which are beneficial to them but also for substances which tend to destroy them. It is through these receptors that bacteria by means of their toxins

and other metabolic products attack the cell. When a cell has been thus set upon and injured, the reparative powers of the body exercise their function and one evidence of repair is the production of more receptors. As nature is prodigal in all her reparative processes an excess of receptors is manufactured and some are crowded out into blood and tissue juices. A large number of these receptors floating in the serum constitutes the antitoxins and antibacterial serums.

There are as many different kinds of receptors as there are substances which attack the cells. The haptophore group (as it is called), of the toxin or poison must exactly fit the receptor or there is no toxic effect produced. The mongoose is not affected by a snake bite, in other words, the cells of the mongoose have no receptors which fit the haptophore group of snake venom.

This brings us to the place which the opsonic theory of Wright occupies in the study of immunity. For a number of years the French school, with Metchnikoff at its head, has been maintaining that the formed elements of the body are responsible for resistance to disease, while Ehrlich and the German school contends that the body fluids are of most importance in this connection. Wright has shown that both these elements are almost equally important—the leucocytes ingest and destroy infecting bacteria but are able to do this only after the latter have been acted upon by some substance in the serum of the blood. The substances in the blood and tissue juices which prepare bacteria for phagocytosis have been called opsonins—from a Greek word meaning to prepare for food. Immunity according to this theory depends upon phagocytosis, and phagocytosis depends upon the opsonins. Obviously then the degree of immunity depends upon the opsonic content of the blood. The ingenious technique devised by Wright and his co-workers has facilitated the estimation of these substances.

Definition.—The opsonic index expresses the power of the blood serum of the individual under examination to prepare bacteria for phagocytosis compared with the same power of the blood serum of a healthy individual under exactly the same conditions.

Technique.—To determine the opsonic index three things are necessary:

(1) A suspension of bacteria.

(2) A suspension of healthy leucocytes.

(3) Blood serum.

The last is the only variant.

Equal parts of these are drawn into a capillary pipette; after thorough mixing, the pipette is sealed and the mixture is kept at the body temperature for about fifteen minutes. During this time the opsonins which are contained in the blood serum act upon the bacteria—opsonize them. Those bacteria which have been prepared are then ingested by the leucocytes. After incubation the contents of the pipette are again thoroughly mixed and spread upon slides. The slides are properly stained and examined under the microscope. One hundred leucocytes are counted and the number of bacteria they have ingested is recorded. Two different mixtures are made, one using the blood serum of the patient, the other the blood serum from at least one healthy individual. The opsonic index of the healthy person being taken as 1, the proportion between the number of bacteria ingested in the two cases gives us the opsonic index of the patient. For example: with healthy serum one hundred leucocytes ingest 400 bacteria, with the patient's serum the same number of leucocytes ingest only 300 bacteria, then 400: 300: 1: X. The opsonic index of the patient is 0.75.

If the patient's serum prepared 500 bacteria, his index would be (400: 500: 1: X)—1.25.

One of the important practical features of a knowledge of the opsonic index is its value as an aid in diagnosis.

When a person is infected with a certain organism, the tubercle bacillus, the staphylococcus or whatever it may be, his opsonic index to that particular organism is likely to be below normal, it may be above, or the equilibrium may not be disturbed.

If a patient is suffering with some obscure disease of the throat, for instance, and it is impossible for the laryngologist to decide between cancer or tuberculosis, a tuberculo-opsonic index of, say, 0.75 is almost conclusive evidence of tuberculosis. The diagnostic value of this procedure in obscure surgical diseases cannot be overestimated.

But the most important field the opsonic index has occupied is in control of dosage for vaccine therapy. When the opsonic index is persistently low to a certain organism it shows us that the resistance of the patient is low to infection by this organism, and unless his resistance can be raised in some way we can expect no improvement.

Wright has shown that the opsonic index can be raised if we inject beneath the healthy skin a certain number of killed bacteria of the same variety as those which are infecting the patient. The number of killed bacteria to be injected and the intervals between doses have been carefully studied by Wright and his co-workers. When the proper dose of killed bacteria has been injected there is first a fall in the opsonic index; this is followed by a rise above the normal. The fall in the index is probably due to the neutralization of the opsonins which are in the blood by the injected bacteria—this is called the negative phase. The subsequent rise is called the positive phase, and it is during this period that improvement in the patient's condition is looked for. It is not necessary to give a second dose of killed bacteria so long as the index remains above normal.

These suspensions of killed bacteria are called bacterial vaccines. There has been some discussion as to the use of this word which heretofore has meant, to the popular mind, at least, that material used for the purpose of conferring immunity to smallpox. According to the etymology of the word it is truly a misnomer employed in this general sense, but custom has sanctioned its use.

A vaccine is any material intended for administration with the idea of stimulating the production of active immunity to a certain disease. We vaccinate man to protect him against smallpox; cholera, bubonic plague, typhoid fever; we vaccinate animals to protect them against anthrax, black-leg, erysipelas, rinderpest. Even plants may be vaccinated.

The difference between an antitoxin and a vaccine is that an antitoxin confers passive immunity, while a vaccine stimulates active immunity. The vaccines used to raise the opsonic index and thereby bring about improvement in localized infections are merely bacteria suspended in normal saline solution.

For the preparation of these vaccines, cultures are made upon the surface of a solid culture medium, usually agar-agar. These are kept at the body temperature for about twenty-four hours and the resulting growth washed off with sterile salt solution. The thick suspension is collected in a proper vessel and the bacteria are killed at 60° C. This temperature is just sufficient to destroy the life of the germs with little injury to their specific immunizing properties. The bacterial suspension is now shaken for an hour or more

to break up all clumps (some organisms require special treatment to secure this end), in order that a homogeneous suspension may be obtained. To accurately measure the dose of these vaccines it is necessary to count the number of bacteria per cubic centimeter. This is done by one of Wright's most ingenious methods. Equal volumes of blood and bacteria are measured by means of a capillary pipette and thoroughly mixed, after which a drop of the mixture is spread upon a slide in a thin layer by drawing the edge of another slide over it. The thin film thus prepared is fixed and stained. Under the microscope the red blood corpuscles and bacteria contained in a number of fields from various parts of the slide are separately enumerated. Knowing the number of red corpuscles in one cubic centimeter of the blood used, the proportion between the corpuscles and bacteria being ascertained by this enumeration, it becomes a simple mathematical problem to calculate the number of bacteria per cubic centimeter. For example, in twenty-five fields we find 800 red corpuscles and 1600 bacteria; by one of several well-known methods we have determined that there are 5,000,000 red corpuscles per cubic millimeter or 5,000,000,000 per cubic centimeter—then 800: 1600:: 5,000,000,000: 10,000,000,000.

The next step is to dilute the thick suspension sufficiently to make each cubic centimeter contain a convenient number of bacteria. A small percentage of liquor cresolis comp. (N.F.) is generally added to prevent contamination.

Experience in St. Mary's Hospital appears to favor extremely small doses. Those published a year or more ago are much larger than the numbers given me by Professor Wright during the past summer. These are as follows:

Staphylococcus	50,000,000 to 250,000,000
Streptococcus	1,000,000 " 5,000,000
Gonococcus	500,000 " 2,000,000
Pneumococcus	10,000,000 " 20,000,000
Colon bacillus	5,000,000 " 20,000,000
B. pyocyaneus	5,000,000 " 20,000,000
Micrococcus neoformans	5,000,000 " 100,000,000
Micrococcus catarrhalis	according to turbidity.

The tuberculins are used for the same purpose as bacterial vaccines and in practically the same way. A description of the method of their preparation which is quite different from that of the bacterial vaccines would increase the length of this paper unduly.

As is well known all biological products deteriorate in the course of time. Smallpox vaccine kept at the temperature of the body is valueless after a very few days. According to Elgin it may be kept for years at a temperature of about—5° C. without the least impairment of strength. Our own experiments have shown us that diphtheria antitoxin, under the ordinary conditions of the market, loses about 2 per cent. of its potency per month. When kept at a little above the freezing point the deterioration is practically nil. We have no way of gauging the activity of bacterial vaccines and no method of accurately determining the loss in strength on keeping, but we do know that there is some loss, and we know that temperature and light are the most active influences in this direction. The lesson to be learned from this is that all biological products should be kept as near the freezing point as possible, and the pharmacist who displays packages of antitoxin and vaccines in his shop window, or keeps them in a show case, is what our President might call an undesirable citizen, not so much from the standpoint of the manufacturer, as of the patient who must suffer the result of not receiving the full benefit of a product which had been kept under proper conditions. An efficient refrigerator is absolutely necessary in every drug store which handles biological products. This necessity will increase with the increase of our knowledge of immunity. For specific infections drugs will be used less and less and the use of specific curative and immunizing materials will increase in proportion.

THE OPSONIC THEORY IN RELATION TO TUBERCULOSIS.

By E. Burvill-Holmes,
Bacteriologist, Phipps Institute, Philadelphia.

When I accepted the invitation to appear before you, I was under the impression it was but to discuss the paper of Dr. Hitchens, to which you have just listened. When, three or four days later, I received a printed card announcing that I should read a paper on "The Opsonic Theory in Relation to Tuberculosis," I can assure you it came as a surprise. As a matter of fact, had I been apprised of this in the first place, I should have indubitably declined the honor, and for the one good reason that I should have felt, as I do

feel, very presumptuous in undertaking a task to which I fully appreciate I can do but feeble justice. My personal experience on opsonins in connection with tuberculosis is comparatively limited, more of my work having been done with the organisms responsible for the mixed infections. However, since I shouldered the responsibility of this paper, and you will forbear with me a short time, I will attempt in as brief a manner as possible and as lucidly as my literary abilities will permit, to give you an insight at least into the subject.

Inasmuch as Dr. Hitchens has explained so fully what is meant by "Opsonin" I will not reiterate it. Neither will I tax your minds with the various theories of immunity, of which there are a great number—some simple, others intricate. Any of you who are thirsting after such knowledge and are desirous to wrestle with these problems I can only refer to the many works on the subject of past and recent times. I would not touch upon the technique of estimating the opsonic index in tuberculous patients were it not for the fact that in working with the *Bacillus tuberculosis*, methods are somewhat different than are those when other bacteria are employed. To be sure the preparation of the blood cream is the same in both instances; the contents and proportion of each in the opsonizing tubes do not differ, to the exclusion of the organism used; the process of mixing is the same, as is also the making of the smears. On the other hand, the preparation of the emulsion is a more difficult and tedious task than is the case with the other bacteria if a suitable one is to be obtained; special staining is required and the time of incubation is more prolonged. Let me digress one moment and say a few words here as to the mixing. The method adopted by Wright has been explained to you by Dr. Hitchens. It seems to me that the method while insuring thorough incorporation is, except in very skilled hands, performed at the risk of introducing many air bubbles to the tube, thus interfering with proper phagocytosis. I have observed some laboratory workers indeed, who, in order to avoid this exasperating complication, have abstained from completely emptying the tube at each compression of the rubber nipple, which would of necessity be fruitful of errors. To overcome this I have devised a tube which I have found extremely satisfactory. It is easy to manipulate; thorough mixture is secured, and it obviates, or at least

reduces to a minimum, the possibilities of air bubbles. The tube in question is simply that of Wright's with a small central bulbous swelling. I say small advisedly, because if made with a large bulb, much of its contents are lost on account of its adherence to the sides. To mix the blood cream serum and the emulsion they are passed and repassed through this bulb a dozen or more times, allowing the mixture to collect in the bulb in which it is incubated. It is important that the contents of the control tube and those in the others to be tested should each be passed through the bulb the same number of times.

PREPARING THE EMULSION.

At the Phipps Institute we prepare our emulsions in a manner similar to that adopted by Wright and others. The bacilli from flasks of broth culture filtered through filter paper or a Pasteur filter are washed in water and subsequently with salt solution of a strength of 1·5 per cent. and sterilized. A drop or two of this same strength salt solution is placed in a mortar and a very small mass of bacilli added. The mixture is rubbed up now for ten to fifteen minutes when a drop or two more of the solution is added and the grinding process continued for a few minutes, and so on, until the total amount of emulsion equals about 1 c.c.. This is transferred to a test tube, centrifugalized a few minutes and the supernatant fluid, of a milky opacity free from clumps of the organism, is drawn off and is ready for use. Nevertheless, it is always advisable to make a test of the emulsion before proceeding to employ it for investigations Failure to do this, as I have learned from bitter experience, often means the useless sacrifice of time and labor, to say nothing of the vexation to which one is apt to give vent, in a way that is more. forcible than elegant. Too thick an emulsion renders counting of the bacilli impossible, or at least difficult and uncertain, while, if too sparse the index is materially affected. Kinghorn, Twitchel, Carter and others, in a series of experiments have shown that the phagocytic index is in proportion to the dilution. An emulsion which gives from one to four bacilli to a cell is suitable. It is our custom to prepare it in quantities, a good deal of work being saved thereby. With proper precaution against contamination it can be kept for several days. At Saranac Lake Sanatorium emulsification is brought about by means of a porcelain ball mill. Von Ruch, however,

putting the mill to the test says that he found it wanting, and not one whit better than the more primitive mortar and pestle, to which he has reverted.

STAINING THE SMEAR.

It is unnecessary to fix the smear as is the custom with some, by means of alcohol or other fixative, as the heat to which the slide is exposed during the process of the preliminary staining by carbol fuchsin is sufficient for the purpose. Our method is as follows:

Carbol fuchsin with heat, 2 minutes.
Wash with water.
Decolorize with 25 per cent. sulphuric acid.
Counterstain with borated methyleneblue 30 seconds.

The advantage of this latter counterstain over the much used and popular Loeffler's preparation is that the protoplasm of the cells is stained, which is not the case with either Loeffler's or Gabbet's—the latter a mixture which is both a decolorizer and stain. With the protoplasmic limits undefined one can readily comprehend how errors in computation could be made as it would be impossible, and is impossible, to definitely locate an organism in many instances, in other words to say whether it is within the cell or just without.

Dr. Hitchens has explained to you what constitutes a bacterial vaccine, and how they bring about curative results. In tuberculosis we make use of a vaccine, if one may so term it, called tuberculin, and inasmuch as you may at some time or another be required to know of this remedy I will briefly refer to it. There are several kinds of tuberculin on the market to-day, but when we refer to tuberculin we usually mean one of the three kinds, either the so-called old tuberculin, that known as "TR," or the Bacillen emulsion. All of these were originally the product of Koch's laboratory, but now many laboratories manufacture these for their own use after the Koch formula. The difference between them is that the former is merely a filtered bouillon culture of the bacillus concentrated by heat to one-tenth of its volume while the two latter contain the actual bacterial substance. At the present time these three kinds are being very extensively used.

THE VALUE OF ESTIMATING THE OPSONIC INDEX.

The earlier observations of Wright and Douglas were made with organisms other than the *B. tuberculosis*, and they showed, as you

have already heard, that normal serum contained a bacteriotropic substance which they termed opsonin, and which was specific for the respective organisms. In 1905, before the Royal Society of London, Wright announced how, by means of his technique, it was possible to clear up a questionable diagnosis of tuberculosis, whether as a localized affection or general. His statement was based on much painstaking experiment in which he had for a co-worker Surgeon Reid. Not only did he show how this was possible by examination of the blood of the suspected individual, but also by other body fluids such as pus from a joint or the effusion from the chest or abdominal cavity. That by studying the opsonic power of the blood at least—because seemingly aside from the pioneers in this work little has been done with the other body fluids—a fairly good inference can usually be drawn as to the existence or non-existence of tuberculosis, I think is pretty well agreed on by most workers. A persistently low and uniform reading is usually found in cases of localized tuberculosis such as gland, joint and skin infections. To the contrary, uniformity of curve is rarely observed in conditions marked with constitutional disturbances. At one time it is high, perhaps twice as high as normal, and a little later abnormally low. Wright explains and with reason the difference in the condition of the blood in these two contracted categories in this wise: To quote him, "The condition of low opsonic power which is associated with strictly localized tuberculosis is almost certainly a condition which has preceded and has furnished the opportunity for infection. The fact that the opsonic index continues persistently low after infection has supervened, while it can invariably be raised by appropriate inoculations, indicates that the machinery of immunization with which the organism is furnished, is not, under the condition which obtains in strictly localized tuberculous infections, spontaneously called into play." The fluctuations in cases of active pulmonary tuberculosis he lays to the "periodic conveyance of tuberculous elements into the blood"—an auto-immunization. Here, then, with these facts borne out one can perceive what a valuable asset we have in Wright's discovery. Ross working with Wright pointed out what is considered a most trustworthy test for diagnostic purposes. His results are extremely interesting and seemingly very conclusive. In the course of his investigations he found that normal serum when heated to 60° C. for ten minutes, no longer had the

power of activating the leucocytes. From a tuberculous person, however, in spite of the heating process the appetite of the cells for the bacilli was not at all disturbed.

Again, a probable diagnosis of tuberculosis can be made in those persons who, on receiving even a minute inoculation of tuberculin, respond with a very low opsonic reading. While a negative phase does occur in an individual, who is not tuberculous, it is only after a comparatively large dose, and this negative phase is ephemeral only. What most appeals to one in point of interest and ingenuity, however, is perhaps the method of diagnosis by comparing the serum of the patient with some other of his body fluids. Wright has shown that if the opsonic power of, say, some of the effusion from a patient's chest is much lower than his blood, the effusion is unquestionably tuberculous in character. I shall here take the liberty to intrude upon your valuable time to cite a case illustrating this, and do so, because it is really unique. A man, aged 30 years, showing grave constitutional symptoms baffled his physicians as to his malady. The latter suspected tuberculosis and, accordingly, some of his blood together with some fluid, obtained from his abdomen by tapping was sent to the laboratory. The report from the laboratory was "non-tuberculous," and on the grounds that while the index of the blood was 1·05, the fluid was ·99 or practically the same. The man's condition became worse. The clinicians refuted or at least doubted the diagnosis of those clever laboratory men. The condition was tuberculous unquestionably, they said, and once more blood and fluid were sent for confirmation. But again the laboratory diagnosis came back "non-tuberculous." This time the serum and fluid both revealed an index of 1. The man shortly afterward died, and on post mortem, what to the naked eye appeared as unquestionably tuberculous deposits were found on the peritoneum and the pleurae, much to the chagrin of the laboratory men, and to the delight of the physicians. However, microscopical examination of some of these apparent tubercles showed the typical picture of miliary carcinoma or cancer. Could there possibly have been a more gratifying vindication for these keen laboratory workers. In a recent number of the London *Lancet* we can read further evidences of the prolific work, which is being done in the Department of Therapeutic Immunization of St. Mary's hospital, by Wright and his assistants, and a large number of graphic charts are shown illustrating the various phases in Therapeutic Immunization.

The tables demonstrating the diagnostic and therapeutic problems are intensely interesting. Withal, the determination of the opsonic power of the blood in the hands of Wright, Douglas, and others in England has yielded results as remarkable as they are consistent. Over on this side of the Atlantic, however, such uniform success has not been the rule and consequently the opsonic theory has come in for a good deal of adverse criticism. Personally, while I have frequently obtained classic curves, I must confess, that many of my results have been provokingly disappointing, but that is neither the fault of Dr. Wright, nor his theory. I believe, when men here shall have worked as systematically, as doggedly, and as long as have our English cousins; when they cease to attempt to modify the technique as laid down by Wright, they will undoubtedly be able to produce results as consistent and valuable, and not before. Until we have done this, it is unfair for us to pass judgment. That the dosage of tuberculin can be controlled by opsonic determinations in localized tuberculosis can be shown, but for reasons pointed out in the earlier part of this paper it must be plain to you, why this is out of the question in persons, the victims of active and marked pulmonary lesions. Indeed in my modest opinion, tuberculin, unless given in very small doses is fraught with some danger in this latter type of cases. At the Phipps Institute, the concensus of opinion seems to be in favor of small, very small doses in all cases so treated, and opsonic determinations seem to substantiate this. With such doses, as has been in the past the custom to administer, the patient is continually kept in the negative phase, and not until the dose has been materially diminished do we find an augmentation of the opsonic power. Of course, in the administration of the remedy, the idiosyncrasy of the patient and the questionable strength of the remedy—because, of course, the very nature of it precludes standardization—must not be lost sight of. Aside from purposes of diagnosis, we may eventually find it unnecessary to resort to opsonic indices and as a guide to inoculations it may be relegated to the background. But one thing is certain, and that is that vaccine therapy is here to stay, and sera and vaccines will supplant in many cases pills and potions, which are, alas, too often as useless as they are unpalatable.

PROGRESS IN PHARMACY.

A QUARTERLY REVIEW OF THE MORE IMPORTANT ADVANCES IN PHARMACY AND MATERIA MEDICA.

By M. I. Wilbert,
Apothecary at the German Hospital, Philadelphia.

To one who is at all interested in the progress of the professional side of pharmacy, a retrospect of the meetings of medical and pharmaceutical organizations, during the past year, must indeed be an inspiration and provocative of a justifiable sense of satisfaction.

The proceedings at the annual meeting of the American Medical Association, the American Pharmaceutical Association and of other organizations have been reported at some length in this Journal and are well worth reviewing.

The annual meeting of the National Wholesale Druggists Association held in Denver, Col., the week following October 1st, appears to have been dominated by a careful consideration of legislative matters and the evident need for co-ordinating the several State food and drug laws with the provisions of the National Law.

Considerable attention was also devoted to the consideration of various methods that have been proposed for curtailing and regulating the sale of habit forming drugs and preparations containing them.

The National Association of Retail Druggists, at the annual meeting held in the city of Chicago the week following September 15th, decided to enter upon an active propaganda to popularize U.S.P. and N.F. preparations.

A special meeting of the Association was devoted to the discussion of the problems involved. At this and at the subsequent regular meetings of the Association, much enthusiasm was manifested and the resolutions directing that this work be undertaken were adopted without opposition of any kind.

From an educational, or a professional point of view this proposed propaganda is by far the most important, and the most far reaching, of any line of work undertaken by the National Association.

If carried to a successful issue it will bring with it a very material advance in the ideals and practices of present-day pharmacy, and it will certainly bring about an early realization of that better, if not completely satisfactory, understanding of the mutual duties and

limitations of pharmacists and physicians as outlined by Dr. J. N. McCormack, in his address before the American Pharmaceutical Association, in New York, last September.

This address on the relations of pharmacists and physicians, appears to have been misunderstood, or at least misinterpreted, by some persons who really should know better.

The portion of the address that has been more or less severely criticized is the introduction, consisting largely of a quotation from the report of the committee on organization of the American Association and published, in part at least, in the AMERICAN JOURNAL OF PHARMACY, 1907, page 331.

To any one who has followed the reports of legislative work, in connection with State food and drug legislation, and particularly the work done in connection with the so-called formula-on-the-bottle bills, and at the same time remembers that the physician and the retail druggist look upon the situation from a radically opposite point of view, the strictures made by Dr. McCormack will appeal as being moderate indeed.

Pharmacists, if they wish to pose as professional men, cannot longer avoid their responsibility in connection with the sale of so-called proprietary remedies. They should collectively, and if this is not practicable, they must individually inquire into the nature and composition of the remedies they dispense. If found to be harmful, or not as represented, they can no longer shirk responsibility by hiding under the time-worn excuse that the public demands them and the public demands must be supplied.

It is rather interesting to notice how widespread the present agitation against proprietary and fake remedies has become. The following is from an editorial note by Gnomon (*Phar. Jour.*, London, 1907, page 360.):

"Sooner or later—and sooner, I hope, rather than later—pharmacists and wholesale druggists will recognize that they are equally interested in the suppression of quackery and of attempts to monopolize the trade in medicines by more or less insidious methods.

"There should be a concerted movement in the direction of making it clear to medical practitioners and the public that there is no virtue in secrecy so far as drugs, chemicals and galenical preparations are concerned, and that all the effects obtained by esoteric combinations of well known medicaments can be equally well

obtained by the use of those medicaments under their own proper designation."

An editorial, in the same journal, one week later (September 24th, page 375) says:

"The majority of quack medicines which are advertised as tonics, or by similar alluring names, derive their popularity from the effects of sedative drugs, by which sensations of immediate comfort are imparted to the consumer, and which frequently lay the foundations for a confirmed habit of morphin taking."

A correspondent in the same number says: "It is high time that we disassociate ourselves from trickery, treachery, humbug, fraud and lies." Another correspondent (September 28th, page 427) says: "There is no getting over the fact that, by the actual connivance of some of our members and the passive attitude of others, we are in a high degree aiders and abettors. By no logic can we claim that our hands are clean."

In Germany restrictions on the sale of secret remedies are increasing in number and severity. A recent law just being enforced makes it unlawful for apothecaries or druggists to sell, except the former on the original prescription of a medical man, any medicinal compound the composition of which is unknown by the seller. The law of 1903 compelled proprietors to state ingredients and quantities on each package, but the new law goes much further and forbids all written or printed praise of any proprietary preparation on the label or the literature accompanying the package.

A preliminary list of the prescribed preparations has been published in the pharmaceutical journals. It includes upwards of 150 specialties, some of them of American origin.

American Medical Association, Post-Graduate Course.—As an interesting possibility of what may be accomplished by legitimate organization work, it may be well to call attention to the rather comprehensive course of post-graduate study that has been outlined by the American Medical Association. (*Jour. A. M. A.*, September 21, 1907, page 1043.) So far as outlined the course includes a weekly programme for six months' work, particular attention being paid to treatment and the study of materia medica, pharmacology and therapeutics.

Active Campaign Against Proprietary Medicines.—The Kentucky State Medical Association has undertaken an active campaign

against medical frauds and for legitimate pharmaceuticals, including an active U.S.P. and N.F. propaganda.

The work is being done through the county societies and it is evidently the intention to get every medical practitioner to promise to take an active part in the campaign by getting him to signify his willingness to adhere to official, or honestly exploited remedies and to eschew all remedies of a doubtful or objectionable character.

The House of Delegates of the Kentucky State Medical Association, during the recent meeting in Louisville, also adopted a resolution recommending that the State Legislature pass a bill requiring graduation from a recognized college of pharmacy with its accompanying degree, as a qualifying necessity for permission to enter examination before the State Board for license as registered pharmacist. (*Jour. A. M. A.*, October 26th, page 1466).

Pharmacopœia Helvetica, ed. IV, is the official title of the recently published Swiss pharmacopœia which has been in course of revision for several years. Despite the fact that the several changes that are embodied in the book have been publicly discussed, the completed book has attracted unusual interest in Europe, and particularly in Switzerland, where the pharmacists are justly proud of their achievement in the pharmacopœial line.

The expectation that pharmacy in Switzerland will enter upon a new era of development with the adoption of the new, fourth, edition, of the official pharmacopæia appears to be amply justified by the advances that are evidenced in the book itself.

The new pharmacopœia contains upwards of 200 pages more than the now official third edition. This increase is largely devoted to an elaboration of the descriptions and tests for identity and purity. Assay processes are numerous and the use of the compound microscope will, in future, be obligatory.

The provisions of the International Conference for the Unification of Potent Medicaments have been closely followed; all of the remedies enumerated in the protocol being designated by the addition of the letters (P. I.).

The new pharmacopœia becomes official on March 1, 1908, and will require considerable change in the laboratory facilities of the average pharmacist. To assist Swiss pharmacists to adapt themselves to the requirements of the new pharmacopœia, and to perfect themselves in the necessary technique, in chemistry and microscopy,

Professors Tschirch and Oesterle announce that they will conduct a post-graduate course of instruction, covering about ten days, open to all Swiss pharmacists.

Japanese Pharmacopœia—The English translation of the Japanese pharmacopœia has been published and was reviewed at some length in a recent number of the *Chemist and Druggist.*

A German translation of the new Japanese pharmacopœia has been published in Osaka. This latter translation was made by the Director of the Hygienic Laboratory, at Osaka, Mr. M. Hirayama. (*Phar. Post*, 1907, page 749.)

Pharmaceutical Education in Great Britain.—In an address at the opening of the sixty-sixth session of the School of Pharmacy of the Pharmaceutical Society of Great Britain, Prof. Raphael Mendola, of the Finsbury Technical College, and an honorary member of the Pharmaceutical Society, discoursed on the shortcomings of the scientific education of pharmacists in Great Britain. Comparing the training given British pharmacists with that given on the Continent of Europe, he finds that the former is far behind that of any other country in Europe, with the possible exception of Italy and Portugal.

Professor Mendola believes that the introduction of a course and degree in pharmacy by the Universities of Manchester, Glasgow and Edinburgh, will serve as a leavening influence to bring about the necessary demand for higher qualifications in the practice of pharmacy.

The address has been published in full in the several British Pharmaceutical journals. It is well worth a careful perusal by all American pharmacists and it should certainly be read and reread by all opponents of higher educational requirements.

The Flückiger Gold Medal has been awarded to Prof. Eduard Heckel, the Director of the Colonial Institute at Marseilles. The medal was founded by Dr. F. A. Flückiger, of Strasburg, in 1893, and is awarded every five years, in recognition of steps taken to promote the advancement of scientific pharmacy, irrespective of nationality. Mr. E. M. Holmes, the Curator of the Museums of the Pharmaceutical Society of Great Britain, received the first medal, and the second was presented to Dr. C. Schmidt, of the University of Marburg. (*Phar. Jour.*, September 14, 1907, page 335.)

Cactin and Cactina.—Dr. R. A. Hatcher (*Jour. A. M. A.*, page

1021) reviews the available literature of *Cactus grandiflorus* and records a number of control experiments made with the supposed active principle of the drug.

Hatcher concludes that cactina, as marketed at the present time by the Sultan Drug Company, and cactin, as sold by the Abbott Alkaloidal Company, are absolutely devoid of any action resembling that of digitalis or strychnine, and that they are evidently inert when used on animals in doses that are hundreds, and even thousands, of times as large as those recommended by their exploiters.

Calcidin (*Abbott*).—According to an analysis made in the chemical laboratory of the American Medical Association, this preparation is essentially a mixture of iodin, calcium iodid, lime and cornstarch made by mixing iodin, lime and cornstarch.

According to the makers, "calcidin (Abbott) is an entirely unique substance, being neither a true chemical compound nor a simple mixture of its ingredients. Briefly, it is calcium carrying an excess of freely available iodin." (*Jour. A. M. A.*, September 7, 1907, page 865.)

Calcidin Tablets do not have the same composition as calcidin itself. While 1 grain of the latter was found to contain approximately $\frac{1}{10}$ grain of iodin, three calcidin tablets, which are said to represent 1 grain of calcidin, were found to contain the equivalent of but $\frac{1}{88}$ grain of iodin.

Iodide of Lime (*Nichols*).—An analysis of this substance shows that it is essentially a mixture of lime and iodin, containing about 10 per cent. of the latter.

Iodid of Lime Tablets (*Nicholls*) were found to differ in composition from the original substance, each $\frac{1}{3}$-grain tablet containing the equivalent of $\frac{1}{128}$ grain of free iodin and colored brown by iron oxide. (*Jour. A. M. A.*, November 2, 1907, page 1540.)

Probilin Pills.—From a chemical examination of probilin pills, made for the Council on Pharmacy and Chemistry of the American Medical Association (*Jour. A. M. A.*, August 24, 1907, page 702), it appears that the true composition of this preparation differs materially from the formula, as published at that time, and is about as follows:

Phenolphthalein, 0.008; sodium salicylate, 0.01; sodium oleate and free oleic acid, 0.10; menthol, 0.01; moisture, 0.006; dusting powder, 0.065.

The dusting powder appears to be made up of lycopodium, licorice and charcoal.

Under date of October 5, Messrs. Schering and Glatz publish a revised formula for probilin which practically agrees with the analysis as given above.

Heroin and the Heroin Habit.—It has been claimed for heroin, the diacetylester of morphine, that it is less poisonous than morphine and also that it is generally more efficient and more reliable. According to M. P. Duhem, heroin does not possess any of these advantages. He found it to be fifteen times more poisonous than morphine for rabbits, and believes it to be equally poisonous for man.

He also states that heroin induces to a habit that is even more dangerous and more difficult of treatment than the morphine habit. (*Apotheker Zeitg.*, 1907, page 920, from "Progrès Médica.")

Maretin Poisoning.—The continued use of maretin, an antipyretic formerly exploited by the Farbenfabriken of Elberfeld, even in small doses, has been found to produce a high-grade anaemia accompanied by marked morphologic changes in the blood corpuscles. The danger from this drug is said to lie in its cumulative properties. (*Apotheker Zeitg.*, 1907, page 753.)

Copaiba.—E. J. Parry (*Chem. and Drug.*, September 28, 1907, page 518) asserts that an enormous amount of adulteration of copaiba is being practiced at the present time. The United States have recently rejected a number of parcels of copaiba which had until recently proved good enough for their market as well as the British.

Parry enumerates as a possible adulterant, hardwickia balsam, which has been said to be a commercial article on a large scale. This substance was described in a recent number (April, 1907) of Schimmel's Report, in which it is asserted to be obtained from *Hardwickia Pinata*, a stately tree closely allied to the *Copaifera* species, that is found in British India. Weigel and Hooper have examined the balsam which is said to vary somewhat in physical properties. Schimmel & Co. give the following figures: Specific gravity, 1·0021; acid number, 96·2; ester number, 12·3; content of volatile oil, 44 per cent.

Emulsient is a word that has been suggested as a substitute for the roundabout expression "emulsifying agent" or for the uncouth "emulsifier." (*Chem. and Drug.*, October 12, 1907, page 577.)

Xrayser, in commenting further, says: "It is a term that deserves to survive. It follows precedents, is unambiguous and only competes with admittedly unsatisfactory rivals."

Mistletoe, Viscum Album, formerly had a reputation as a remedy in the treatment of post partem hemorrhage, and the berries are also said to have purgative and emetic properties. It is being reinvestigated in France and is said to have been shown to diminish arterial pressure.

Several pharmaceutical preparations have been prepared from mistletoe growing on poplar and plum trees. These have been brought to the attention of the French Society of Therapeutics by M. Gaultier. (*Chem. and Drug.*, August 31, 1907, page 377.)

Sarsaparilla.—In a recent number of the *Berichte der Deutschen Pharmaceutischen Gesellschaft* (1907, No. 6), C. Hartwich discusses the great uncertainty of our knowledge of sarsaparilla and points out that a number of distinctions formerly given much weight, have been altered materially in the course of time.

Hartwich points out that the structural characteristics of sarsaparilla, rather than the form of packing and the supposed origin, are to be depended on to distinguish the several varieties of the drug.

He also shows that the varieties of sarsaparilla are more numerous than is generally supposed.

Regeneration of Formaldehyde.—Huber and Bickel (*Munch. Med. Woch. schr.*, 1907, page 1800) recommend freshly calcined lime, formaldehyde solution and boiling water for disinfection.

Three liters of the solution of formaldehyde, 3 kilo. of freshly calcined lime and 9 liters of boiling water are mixed in a suitable tub or iron vessel.

The authors claim that but a small fraction of the formaldehyde is lost by combining with the lime, and that the technique affords a simple, cheap and harmless substitute for the more efficient spray technique when the latter is not available or is otherwise objectionable.

Autan.—This is a mixture, in powder form, of a metallic peroxid and paraform. When mixed with a given quantity of hot water a rather violent reaction takes place, liberating formaldehyde and water vapor. (*Chem. Zeitg. Rept.*, 1907, page 376.)

Acetylenetetrachlorid.—This is an aromatic oily substance having a boiling point of 145° C. On account of its high boiling-point it

is being widely used as a solvent in chemical and technical industries, being particularly well adapted for the recrystallization of the chemicals soluble in it. It is also used in rubber industries as a solvent for resinous substances, and has latterly been recommended as an insecticide, being less poisonous and less volatile than other chlorin preparations. (*Phar. Zeitg.*, 1907, page 704.)

Aesco chinin is said to be a combination of the active principles of the horse-chestnut with quinine. The preparation occurs as a yellowish amorphous powder, insoluble in water and ether but readily soluble in alcohol. It is said to be useful in neuralgia, migraine and rheumatism and is given in doses of 0·10 to 0·20.

Escalin Pastilles.—According to F. Zernik (*Apothek. Zeitg.*, 1907, page 918), each pastille contains approximately 2·5 grammes of finely powdered metallic aluminum, 1·5 grammes of glycerin, and 1·0 of distilled water. They are recommended by the makers as being useful in cases of hemorrhage from the stomach or intestine. They are supposed to act purely mechanically by causing a thin coating of the metallic powder to be distributed over the mucous lining of the internal organs.

Formobor.—This is the name given to an aqueous solution containing 4 per cent. of formaldehyde and 1·5 per cent. of borax. The mixture is being recommended as a disinfectant and for sterilizing instruments. (*Phar. Zent. H.*, 1907, page 742.)

Hydrocaffeine is a derivative of caffeine identical with tri-methyl uric acid, in combination with sodium benzoate. It occurs in needle-shaped crystals which sublime at 345° C. The substance is readily soluble in water but is only slightly soluble in alcohol, ether and chloroform. It is recommended as a diuretic in doses of 0·5 gramme. (*Chem. and Drug.*, 1907, page 576.)

Jatrevine is a condensation product of menthol and isobutyl phenol. It is recommended to be used in cases of pulmonary tuberculosis. (*Chem. and Drug.*, 1907, page 576.)

Kolatin is a crystalline substance that has been isolated from kola nuts by Goris. Kolatin is a phenol combination having the formula $C_8H_{10}O_4$. It has tannin-like properties and crystallizes in prismatic needles. (*Phar. Zent. H.*, 1907, page 707.)

Sodium Anilarsenate has been recommended by Hallopeau for hypodermic injections in syphilis. It is said to be more efficient, in many cases, than mercury or iodine. Sodium anilarsenate is not to be confounded with atoxyl. (*Phar. Zent. H.*, 1907, page 766.)

Sulphoid is a trade name for a colloidal form of sulphur prepared according to a patented process in which precipitated sulphur is made in the presence of a colloidal body such as albumen, the mixture being constantly agitated during precipitation.

Sulphoid is a grayish white powder containing 80 per cent. of sulphur and 20 per cent. of albumen. It is said to be insoluble in alcohol, ether, acetone and similar solvents, but is said to be soluble in normal saline solution, the solution being precipitated by acids. The substance is being marketed in the form of soap, head pomade and ointment, each containing 10 per cent. of sulphoid. (*Chem. and Drug.*, 1907, page 576.)

Tannothymal is a combination of tannin-thymol-methan, that is being recommended as an antidiarrhœic. It occurs as a whitish gray to reddish gray, odorless and nearly tasteless powder. It is somewhat astringent and is decomposed at higher temperatures. Tannothymal is nearly insoluble in water and is only slightly soluble in ether or chloroform. (*Phar. Zeitg.*, 1907, page 690.)

Thiodine is the trade name for thiosinamine ethyl iodide. It occurs as white crystals having a melting point of 68° C. It is readily soluble in water but only slightly soluble in alcohol. Thiodine has been recommended as being useful in syphilitic affections and in tabes and may be given in doses of 0·10 twice a day, preferably in pill form. (*Phar. Zeitg.*, 1907, page 429.)

Urogosan is said to be a combination of formalin with gonosan that has been found useful in the treatment of septic conditions of the bladder, especially those arising from gonorrheal infection. (*Phar. Jour.*, September 14, 1907, page 359.)

CORRESPONDENCE.

SYNTHETIC CAMPHOR, REPLY TO CRITICISMS.

Professor Henry Kraemer,

DEAR SIR:—In reply to the criticisms made by Mr. Frank Tutin relative to structural formulas contained in my paper on "Synthetic Camphor," I wish to state that these formulas were employed with some misgivings, because of the large number that had been suggested or advocated during recent years, and concerning which

there is at present little unanimity among chemists, excepting camphor. It was deemed advisable, however, to indicate the chief steps involved by using some formulas. Criticisms were expected. Bredt's formula for camphor and pinene were intended to be used. The formula for camphor as it appears in the article is incorrect. The error was noticed in the proof and corrected, but, for some reason, the printer did not make the necessary change. The adjacent CO and CH_2 groups are interchanged and should be transposed.

It is true that a number of investigations have been made since Bredt suggested his structural formula for pinene, but the best that can be said for same is that the formula suggested by Wagner (the one claimed by Mr. Tutin, "now generally accepted") is indicated. Concerning this formula, F. Heusler, in his book translated by F. J. Pond, entitled "Chemistry of the Terpenes," page 47, makes the following statement:

"In the critical consideration of the constitutional formulas of pinene, and other members of the terpene series, which have been advanced by G. Wagner during the course of his investigations above referred to, the incompleteness of the experimental foundations for these formulas, as is sufficiently observed from what has been mentioned, must not be neglected."

Relative to the criticism of structural formulas for camphor and pinene, appearing upon page 353, it is only necessary to state that they are the ones used in the patent, and represent the ideas of one investigator.

Very few chemists have ventured to suggest structural formulas for either borneol or isoborneol. Those used in my communication will be found in an article published by Dr. W. Gössling in the *Pharmazeutische Post*, Volume 38, page 599. So far as I know no criticism has appeared in subsequent numbers of the *Pharmazeutische Post* or other literature relative to these formulas. The criticisms of Mr. Tutin, excepting the correction in the camphor formula are, in my opinion, not well founded.

Respectfully,

L. F. KEBLER.

WASHINGTON, D. C., December 2, 1907.

NOVEMBER PHARMACEUTICAL MEETING.

The regular pharmaceutical meeting of the Philadelphia College of Pharmacy was held Tuesday afternoon, November 19th, with President Howard B. French in the chair, who said in part in introducing the speakers:

"The addresses to-day deal with theories which are comparatively new, but which are exceedingly interesting from the point of view of the research worker."

The meeting was well attended, and was devoted principally to a symposium on the "Opsonic Theory" and its application in the treatment of infections.

Dr. A. Parker Hitchens, of Glenolden, Pa., who spent the past summer working in the laboratory of Sir A. E. Wright, of England, the author of the Opsonic Theory, read an interesting paper entitled "The Opsonic Theory and Bacterial Vaccines." (See page 556.)

Dr. E. Burvill-Holmes, bacteriologist of the Phipps Institute, Philadelphia, an institution designed for the study and treatment of tuberculosis, read a somewhat technical, but instructive paper on "The Opsonic Theory and its Relation to Tuberculosis," which is published in this number of this JOURNAL (p. 563). Two points emphasized by Dr. Burvill-Holmes were smallness of dose of the bacterial vaccines and a strict adherence to the technique worked out by Wright and some other investigators.

It was brought out in the general discussion that while the field of the so-called vaccine therapy is a promising one, and that while the vaccines have been shown to have a value in certain diseases, particularly those of a localized character, and in the hands of those who are able to carry out the technique involved in determining the opsonic index, there is need of conservatism in their application.

Dr. Burvill-Holmes when asked as to the results of the treatment at Phipps Institute, said that he preferred to occupy a conservative position. He said that the patients in the hospital at Phipps Institute had tuberculosis in a more or less advanced stage, as only those known to have the disease were admitted, and that some of them were benefited and others not. In the dispensary of the Institute, on the other hand, Dr. Burvill-Holmes said that a fair measure of success had been attained.

Dr. John M. Swan, of the Polyclinic Hospital, Philadelphia, said that he had visited Wright's Laboratory and his clinics at St. Mary's

Hospital, London, and that he had spent about eight hours there. He said that he would not undertake to discuss the value of the opsonic theory, but would only give the impressions received when he visited Dr. Wright. A large number of patients attend the clinics at St. Mary's Hospital, the majority of whom are sufler. ing from tuberculosis of the bones, joints and lymphnodes.

To these one injection of tuberculin is administered about every ten days. He said that the spectacle was truly impressive, and that the results in the hands of those who are devoting themselves to this special work are really remarkable. Dr. Swan said, however, that he did not witness an instance in which a patient with pulmonary tuberculosis was treated, but that some patients with pulmonary tuberculosis had been treated in the wards of the hospital.

M. I. Wilbert, Ph. M., said that in a letter recently published in the *Journal of the American Medical Association* (November 16, 1907, p. 1690), Dr. Reid Hunt reports that in Ehrlich's laboratory special attention is now being given to the study of "new drugs of definite chemical composition."

Others taking part in the discussion were Professors Remington and Lowe, and Messrs. W. A. Pearson and E. M. Boring.

The programme concluded with a resumé of recent advances in pharmacy by Mr. Wilbert. (See page 570.)

FLORENCE YAPLE,
Secretary pro tem.

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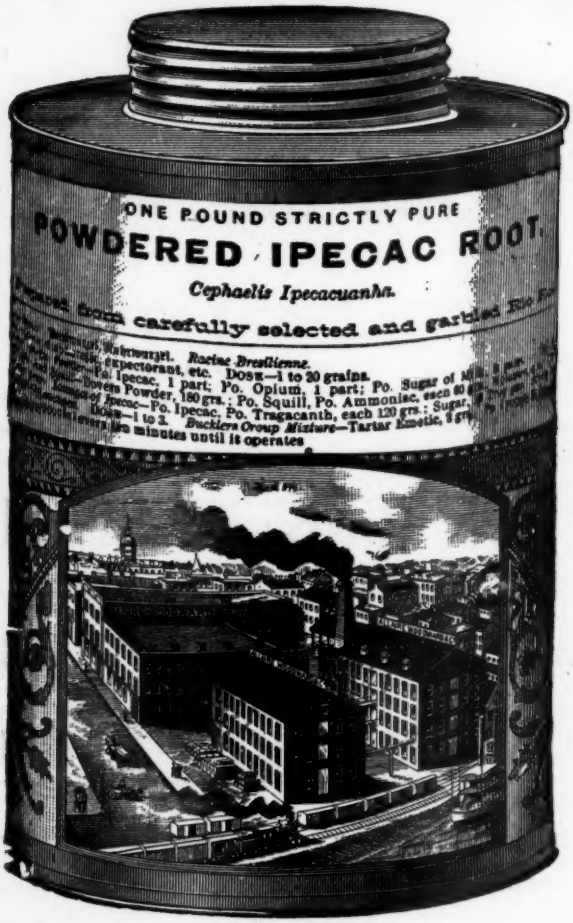
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